Microtesla Magnetic Resonance

A way to acquire chemical information with magnetic fields a million times weaker than those used in typical nuclear magnetic resonance (NMR) spectroscopy has been developed by a team led by John Clarke and Alexander Pines.

NMR and its near relative, magnetic resonance imaging (MRI), are essential tools of scientific research and medical diagnosis. All magnetic resonance techniques depend on the tiny magnetic fields that the nuclei of certain elements (e.g. hydrogen, the ^{13}C isotope of carbon, and the ^{31}P isotope of phosphorus) possess. These fields can be aligned by the application of an external magnetic field and then knocked off axis by a burst of radio waves. This causes the nuclei to "precess" around the direction of the external field; the precession frequencies can be measured by an appropriate detector. The rate at which the nuclei precess is unique; for example, a hydrogen nucleus (^{1}H) precesses four times faster than ^{13}C nucleus. In addition, the chemical environment around the nuclei influences their frequency, causing the "chemical shifts" and patterns of line splitting that are the basis of NMR spectroscopy. In general, these effects scale linearly with magnetic field, such that, for the best resolution, it is desired to perform NMR and MRI with very large magnetic fields (typical fields are one the order of one tesla or 30,000 times the Earth's magnetic field strength).

However, for many potential magnetic resonance applications, it may be impractical to place the object of study in the bore of a high-field magnet. Certain heterogeneous samples, such as organisms studied by *in vivo* spectroscopy, or porous rocks encountered in oil well logging, also present challenges for NMR because, even if they are placed in homogeneous magnetic field, the internal variations in their magnetic susceptibility causes the local field to vary over the sample volume; these variations broaden the resonance lines, leading to loss of chemical information.

Both these challenges can be addressed by developing new NMR techniques that use ultrasmall magnetic fields. Previously, methods had been developed to obtain NMR spectra with field strengths in the millitesla range (see Highlight 99-1). The researchers realized that the linewidth broadening produced by sample inhomogenity scales linearly with the field and thus can be reduced to very low levels by the use of microtesla fields 1000x smaller than those used previously. A major challenge in using ultrasmall fields is that, under ordinary thermal conditions, the concentration of detectable nuclei becomes too small to detect. The researchers overcame this potential problem by "prepolarizing" the nuclei with a brief exposure to a field in the millitesla range and then observing the signal with a relatively inhomogeneous field in the microtesla range using a specially designed and supersensitive superconducting quantum interference device, or SQUID, as the detector. To analyze liquids at room temperature, the team heated their samples in an insulated chamber surrounded by the liquid-helium-cooled pick-up coils of the SQUID.

In a first test, the researchers obtained a spectrum of phosphoric acid (H_3PO_4). As they had predicted, the linewidths of the peaks from hydrogen and the ^{31}P isotope of phosphorus were extremely narrow compared high field spectra. However, as expected, no chemical shift information could be resolved (i.e., there was only one peak for each element). However, there are other internuclear couplings that are field independent and can also be used to obtain chemical information. Specifically, so-called scalar coupling (or J coupling), which is mediated by the quantum states of shared electrons in chemical bonds is such a phenomenon. To test this, the spectrum of tri-methyl phosphate [$PO(OCH_3)_3$] was examined in detail at a field of 4.8 microtesla. In this molecule, the phosphorous is surrounded by nine equivalent hydrogens on the methoxy groups. It was observed that, indeed, scalar coupling between these hydrogens and ^{31}P caused the hydrogen NMR signal to split into two peaks (see figure).

The results show that NMR techniques can be used to obtain information about chemical bonds even in very low and inhomogeneous magnetic fields. The new technique opens the door to chemical sampling even when magnetic signals are heterogeneous, as in living organisms or porous rocks. Additional potential developments of the technique are possible by combining MRI with direct detection of chemical bonds, yielding new ways to investigate processes in brain chemistry and other *in-vivo* systems.

Robert McDermott, Andreas H. Trabesinger, Michael Mück, Erwin L. Hahn, Alexander Pines, and John Clarke, "Liquid-State NMR and Scalar Couplings in Microtesla Magnetic Fields," *Science* **295**, 2247-2249 (2002) and associated editorial, R. F. Service, "Whisper of Magnetism Tells Molecules Apart," *ibid.*, p. 2195.